The X-ray crystal structure of the *trans-dl*-1,2-diaminocyclohexane-(*N*-methyliminodiacetato)platinum(II) complex

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Abstract

The crystal structure of the *trans-dl*-1,2-diaminocyclohexane(*N*-methyliminodiacetato)platinum(II) complex has been determined by X-ray diffraction. It has the following parameters: space group $P2_1/c$ (monoclinic), $a=11.272(5)$, $b=14.034(7)$, $c=10.163(5)$ Å, $\beta=116.13(3)°$, $Z=4$. The slightly distorted square plane of the Pt includes two nitrogens of the diamine in *cis* positions and one oxygen and one nitrogen from *N*-methyliminodiacetate ion. The Pt–N and Pt–O distances average 2.038 and 2.013 Å, respectively. An intricate system of hydrogen bonds which involves every hydrogen atom not attached to carbon was observed. The molecule is a zwitterion and the charge density on the unbound carboxylate is probably stabilized through this series of strong hydrogen bonds.

Introduction

1,2-Diaminocyclohexane platinum(II) complexes with N-substituted iminodiacetates as leaving groups have been reported to have good antitumor activities. In some cases, they were reported to be more active than the parent drug, *cis*-diamminedichloroplatinum(II) (CDDP) [1, 2]. These compounds were less nephrotoxic than CDDP and water-soluble. Furthermore, they were non-cross-resistant with CDDP. However, the structure of these compounds could not easily be established [3, 4]. There are at least two ways that the N-substituted iminodiacetate ion can bind to the platinum(II) atom. Chelation could occur through one acetate oxygen donor and the imino nitrogen, forming a five-membered-ring or through the two acetate oxygens, giving an eight-membered-ring.

Recently, we reported a detailed spectroscopic investigation that showed that the N-substituted iminodiacetate ion binds to the platinum(II) ion through one of the acetate oxygens and the imino nitrogen [5]. The second acetate ion did not participate in chelating. Furthermore, two diastereomers have been observed that corresponded to the two different orientations of the unbound acetate an the alkyl group with respect to the platinum coordination plane.

In this paper, we describe the X-ray crystal structure of one of these compounds, *trans-dl*-1,2-diaminocyclohexane(*N*-methyliminodiacetato)platinum(II).

Experimental

Preparation

trans-dl-1,2-Diaminocyclohexane(*N*-methyliminodiacetato)platinum(II) was prepared by a previously published method [5]. This compound (200 mg) was dissolved in deionized water (20 ml) and left at room temperature to recrystallize. Colorless crystals were obtained.

Crystallographic measurements and structural resolution

A very thin, clear, colorless, flat-column crystal having approximate dimensions 0.07×0.21×0.73 mm was mounted on a glass fiber in a random orientation on a Nicolet R3m/V automatic diffractometer. The radiation used was Mo Kα monochromatized by a highly ordered graphite crystal. Final cell constants, as well as other information pertinent to data collection and refinement, are listed in Table 1. The Laue symmetry was determined to be $2/m$, and from the systematic absences noted, the space group was unambiguously shown to be $P2_1/c$. Intensities were measured using the omega scan technique, with the scan rate depending

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TABLE 1. Data collection and processing parameters

Molecular formula	$C_{11}H_{21}N_3O_4Pt \cdot H_2O$
Formula weight	472.46
Space group	$P2_1/c$ (monoclinic)
Cell constants	
a (Å)	11.272(5)
b (Å)	14.034(7)
c (Å)	10.163(5)
β (°)	116.14(3)
V (Å^3)	1443
Formula units per cell, Z	4
Density, ρ (g cm^{-3})	2.17
Absorption coefficient, μ (cm^{-1})	98.4
Radiation (Mo Kα), λ (Å)	0.71073
Collection range (°)	$4 \leq 2\theta \leq 50$
Scan width, $\Delta\theta$ (°)	$1.30 + (K\alpha_2 - K\alpha_1)$
Scan speed range (° min^{-1})	1.5–15.0
Total data collected	2363
Independent data, $I > 3\sigma(I)$	1937
Total variables	185
R	0.031
R_w	0.033
Weights, W	$\sigma(F)^{-2}$

on the count obtained in rapid pre-scans of each reflection. Two standard reflections were monitored after every 2 h or every 100 data collected, and these data showed a linear decay of about 7% over the course of the experiment. A normalizing factor as a function of X-ray exposure time was applied to the data to account for this decay. During data reduction, Lorentz and polarization corrections were applied, as well as an empirical absorption correction based on psi scans of ten reflections having χ values between 70 and 90°.

The structure was solved by interpretation of the Patterson map, revealing the position of the Pt atom. The remaining non-hydrogen atoms were located in subsequent difference Fourier syntheses. The usual sequence of isotropic and anisotropic refinement was followed, after which all hydrogens were entered in ideal calculated positions and constrained to riding motion, with a single variable isotropic temperature factor. A water molecule of solvation was also found and approximate hydrogen positions determined. Since the hydrogens refined poorly, the entire water molecule was replaced with a rigid-body model having ideal distances and angles. This unit was allowed to refine freely, which led to a reasonable hydrogen-bonding network. The molecules arrange themselves in pairs in the crystal lattice, with one *l*-DACH unit and one *d*-DACH unit mutually hydrogen-bonded across inversion centers. After all shift/e.s.d. ratios became less than 0.1, convergence was reached at the agreement factors listed in Table 1. No unusually high correlations were noted among any of the variables in the last cycle of full-matrix least-squares refinement, and the final difference density map showed a maximum peak of about 1.2 e/Å^3, located near the platinum atom. All calculations were made using Nicolet's SHELXTL PLUS (1987) series of crystallographic programs.

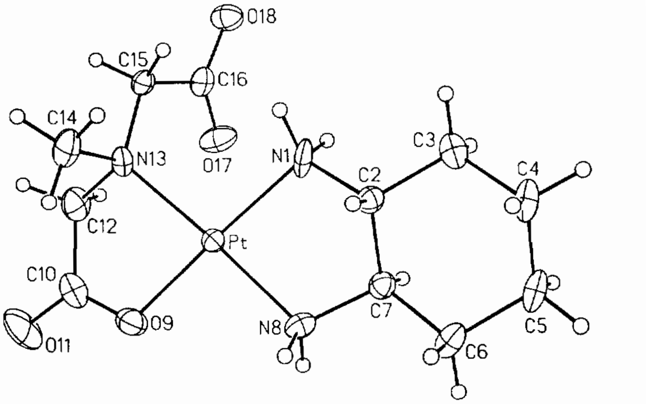

Fig. 1. View of the molecule, with atom labeling scheme. The thermal ellipsoids are 40% equiprobability envelopes, with hydrogens as spheres of arbitrary diameter.

TABLE 2. Bond angles (°)

N1–Pt–N8	83.3(3)
N1–Pt–O9	177.4(3)
N8–Pt–O9	94.9(3)
N1–Pt–N13	98.9(3)
N8–Pt–N13	174.3(3)
O9–Pt–N13	83.1(3)
Pt–N1–C2	108.6(6)
N1–C2–C3	113.2(8)
N1–C2–C7	106.1(8)
C3–C2–C7	110.9(7)
C2–C3–C4	109.7(9)
C3–C4–C5	110.2(10)
C4–C5–C6	112.3(7)
C5–C6–C7	110.2(9)
C2–C7–C6	109.8(9)
C2–C7–N8	108.0(7)
C6–C7–N8	113.1(8)
Pt–N8–C7	110.1(6)
Pt–O9–C10	113.9(8)
O9–C10–O11	123.2(12)
O9–C10–C12	116.9(11)
O11–C10–C12	119.9(9)
C10–C12–N13	111.0(8)
Pt–N13–C12	105.2(6)
Pt–N13–C14	106.4(5)
C12–N13–C14	108.3(8)
Pt–N13–C15	119.7(5)
C12–N13–C15	110.5(7)
C14–N13–C15	106.3(8)
N13–C15–C16	117.0(8)
C15–C16–O17	120.5(10)
C15–C16–O18	113.2(9)
C17–C16–O18	126.3(8)

Results and discussion

The crystal structure of the chelate *trans-dl*-1,2-diaminocyclohexane(*N*-methyliminodiacetato)platinum(II) is shown in Fig. 1, which also defines the labeling of the atoms of the compound. Two adjacent corners of the platinum plane are occupied by the nitrogens of the *trans-dl*-1,2-diaminocyclohexane ligand, whereas the remaining *cis* positions are used to bind one oxygen and the nitrogen of the *N*-methyliminodiacetate group. Coordination about Pt is thus a slightly distorted square plane, with angles ranging from 83.1 to 98.9° (Table 2). The distortion appears to be caused by limitations in the bite distances of the chelating ligands. The Pt–N distances (av. 2.038 Å) are consistent with those found for carboxylate-containing compounds in Pt(oxalato)(1*R*,2*R*-cyclohexanediamine) (2.05 Å), Pt(malonato)(1*R*,2*R*-cyclohexanediamine) (2.04 Å) [6], and *cis*-(diamino)(1,1-cyclobutanedicarboxylato)platinum(II) (2.01 Å) [7], for instance. The Pt–O distance (2.013 Å) is also normal compared with values observed in other platinum(II) compounds, such as bis(acetato)-(*trans*)-1,2-diaminocyclohexane)platinum(II) (2.01 Å) [8] and *cis*-(diamino)(1,1-cyclobutanedicarboxylato)-platinum(II) (2.029 Å). There does not appear to be any obvious *trans* influence involving the formal Pt–O bond, since the Pt–N bond lengths are all essentially equal (Table 3).

TABLE 3. Bond lengths (Å)

Pt–N1	2.040(9)
Pt–N8	2.028(6)
Pt–O9	2.013(9)
Pt–N13	2.047(7)
N1–C2	1.495(10)
C2–C3	1.494(16)
C2–C7	1.520(16)
C3–C4	1.530(13)
C4–C5	1.515(17)
C5–C6	1.510(17)
C6–C7	1.523(12)
C7–N8	1.467(14)
O9–C10	1.296(11)
C10–O11	1.226(17)
C10–C12	1.504(18)
C12–N13	1.496(16)
N13–C14	1.510(11)
N13–C15	1.466(14)
C15–C16	1.523(12)
C16–O17	1.227(14)
C16–O18	1.252(14)

trans-dl-1,2-Diaminocyclohexane and *N*-methyliminodiacetate bidentates impose an N1–Pt–N8 angle of 83.3° and an O9–Pt–N13 angle of 83.1° with the platinum atom, which is typical of five-membered rings having similar donor atoms. However, the Pt–N13–C15 bond angle, 119.7°, is much larger than the expected tetrahedral value of 110°, and the angle at C15 (N13–C15–C16 117.0°), is also large. Therefore, there must be some steric strain in the positioning of this side group, possibly exacerbated by the strong hydrogen bonding shown in Fig. 2.

The configuration of the *trans-dl*-1,2-diaminocyclohexane molecule in this study agrees with the previously reported chair configuration of the *d*- and *l*-isomers of cyclohexanediamine [8–11]. The chelate ring formed from *trans-l*-1,2-diaminocyclohexane is puckered with a 'λ' conformation, as evidenced from the negative N1–C2–C7–N8 angle (−53.3°), while the *d*-cyclohexane has a 'δ' conformation.

The molecule shown in Fig. 1 is a zwitterion. The charge density on the unbound carboxylate group is probably stabilized by an intricate series of strong hydrogen bonds, which involves every hydrogen atom not attached to carbon (Table 4). We assume the interstitial water molecules are very tightly bound, since the crystal shows only slow decomposition upon removal from the mother liquor.

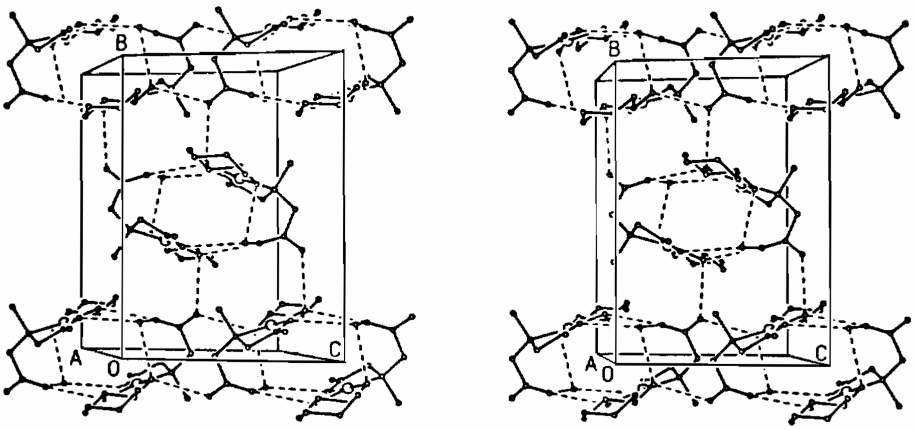

Fig. 2. View of the molecular packing in the unit cell, with hydrogens omitted for clarity. Those atoms participating in hydrogen bonding are connected by dashed lines.

TABLE 4. Distances (Å) and angles (°) associated with hydrogen bonds

A–B ⋯ C	A–B	A ⋯ C	B ⋯ C	<B
N1,H(1A),O18	0.96	2.85	1.90	175
N1,H(1B),O19	0.96	2.93	1.98	170
N8,H(8A),O17′	0.96	2.91	2.06	147
N8,H(8B),O18′	0.96	2.89	1.94	170
O19,H(19A),O17	0.95	3.01	2.17	147
O19,H(19B),O9′	0.95	2.94	2.13	143

Figure 2 shows a stereoscopic view of the molecular packing in the unit cell with hydrogens omitted for clarity. Both *l*- and *d*-DACH moieties occur with equal frequency. Hydrogen bonds are indicated by dashed lines.

Supplementary material

Observed and calculated structure factors as well as anisotropic thermal parameters and hydrogen atomic coordinates can be obtained from the authors on request.

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